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Outcome of paediatric acute flaccid myelitis associated with enterovirus D68

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**Paediatric cluster of acute flaccid myelitis in Scotland
associated with enterovirus D68 (EV-D68) infection and
outcome at 18 months.**

Journal:	<i>Developmental Medicine & Child Neurology</i>
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Keywords:	EV-D68, AFM in Children, AFM and enterovirus, Acute Flaccid Myelitis, Acute Flaccid Paralysis

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[1 Case Series; 2 Figures, 1 Table, 2 Appendix online-only]

Outcome of paediatric acute flaccid myelitis associated with enterovirus D68 (EV-D68): a case series

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***See Appendix S1 (online supporting information) for names and affiliations of the NHS Lothian EV-D68 associated AFM study group.**

PUBLICATION DATA

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ABBREVIATIONS

AFM Acute flaccid myelitis

EV-D68 Enterovirus D68

NPA Nasopharyngeal aspirate

[Abstract]

Enterovirus D68 (EV-D68) is an emerging infection associated with acute flaccid myelitis (AFM). Cases of AFM associated with EV-D68 infection have increased in recent years and the evidence for a causal link is growing. However, our understanding of the epidemiology, clinical features, prognosis, and neurological sequelae of EV-D68 requires ongoing surveillance and investigation. We report five cases of AFM in previously typically developing children (2–6y) from South East Scotland during September and October 2016 after infection with EV-D68 (all detected in the nasopharyngeal aspirates). All cases presented with significant neurological symptoms, which were severe in two cases requiring intensive care support because of respiratory paralysis. At 18 months follow-up, two cases remain ventilator-dependent with other cases requiring ongoing community rehabilitation. These cases represent one of the largest reported paediatric cluster of AFM associated with EV-D68 in Europe. The epidemiology and clinical information add to the knowledge base and the 18 months outcome will help clinicians to counsel families.

What this paper adds:

- Nasopharyngeal aspirate is more sensitive for viral isolation and isolated in all cases.
- Clinical outcome at 18 months after enterovirus D68 with acute flaccid myelitis provides information on extent of recovery and level of disability.

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Developmental Medicine & Child Neurology 2018; XX: 000–000

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Case Series

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[main text]

Acute flaccid myelitis (AFM) is a clinical syndrome, characterized by weakness in one or more limbs with or without respiratory and bulbar muscle weakness, with no specific treatment. There are a number of viruses associated with AFM including polio, enterovirus A71, and flaviviruses.^{1–3} The European region was declared polio-free in 2002.^{4,5} Enterovirus A71 has been linked with outbreaks of AFM recently.^{6,7} Other non-polio enteroviruses have also been associated with AFM but more recently cases of AFM associated with Enterovirus D68 (EV-D68) have been reported.^{8–11}

Since its discovery in 1962, EV-D68 has been associated with sporadic cases of respiratory disease and minor outbreaks worldwide.¹² However, in 2014, the USA declared a nationwide outbreak and reported cases worldwide of over 2000 confirmed cases of EV-D68.^{10,13} There was an increased incidence of AFM during these EV-D68 outbreaks and the evidence for causality has increased significantly.^{9,14,15} In the UK, a cluster of neurological illness associated with EV-D68 was reported in South Wales in 2016.¹¹ There is a paucity of information available about the long-term prognosis and recovery from AFM associated with EV-D68 infection.

We report a cluster of AFM associated with EV-D68 in children with their clinical presentations, public health investigations, diagnosis, management, and outcome at 18 months. This case series will strengthen the existing literature; the clinical outcome at 18 months could help clinicians and families to target interventions.

METHOD

After one case of AFM associated with EV-D68 infection presented to the Royal Hospital for Sick Children Edinburgh on September 10th, 2016, a multidisciplinary incident management team was convened to investigate and set up monitoring for further possible cases. A clinical alert was sent to paediatric services throughout Scotland to be aware of potential cases of AFM associated with EV-D68 infection and to report all possible cases to the incident management team.

The following case definitions for AFM associated with EV-D68 infection were used for identifying subsequent cases after September 10th, 2016.

Possible Case: Person presenting with AFM in Scotland from September 10th, 2016 without other identified cause.

Confirmed Case: Person presenting with AFM in Scotland from September 10th, 2016 with laboratory confirmed EV-D68

Parents of cases were interviewed using a trawling questionnaire (Appendix S2, online supporting information) based on recall and covered exposures within 4 weeks before onset of

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symptoms. All confirmed cases were managed by paediatric neurology and intensive care specialists at the Royal Hospital for Sick Children Edinburgh.

Clinical investigations included brain and spine magnetic resonance imaging (MRI), electrophysiological studies, cerebrospinal fluid analysis, and virology testing (stool samples, throat swabs and nasopharyngeal aspirates [NPA] for a panel of viruses including EV-D6) using real time polymerase chain reaction. Stool specimens were all tested for the presence of polio virus. Fairly extensive neuroinflammatory investigations were carried out in the first two cases and not done in subsequent cases as the diagnosis became more apparent.

All children were regularly followed up by paediatric neurology, respiratory, physiotherapy, occupational therapy, speech and language therapy, psychology, and dietetic teams over the following 18 months. Data on this follow-up period were extracted from clinical records.

Parents gave written consent for the use of anonymised data for investigation and dissemination. NHS Lothian Caldicott Guardian's approval was obtained for data storage and dissemination.

RESULTS

Clinical presentation and epidemiology

All confirmed cases were residents within the South East Scotland region. Figure 1 displays the chronology of onset of prodromal and neurological symptoms for this cluster. From the questionnaires, there were no common sources (food, environmental exposures, recent travel, and previous direct contact with each other) identified. All children had received age-appropriate vaccinations, including inactivated polio vaccine. Their prodromal illness, clinical presentation, neurological weakness, investigations, treatment, and progress have been detailed in Table I. All presented with asymmetric flaccid weakness of varying severity, severe pain, three with bulbar involvement, and the two severely affected cases required intubation and respiratory support.

Investigations

All confirmed cases had EV-D68 detected from NPA samples after their admission. Two tested positive for EV-D68 on throat swab. However, in one case repeated throat swabs were negative and only confirmed on NPA. Viral typing confirmed EV-D68 B3 lineage. Faecal testing for polio was negative in all cases.

All children had a brain and spinal MRI and demonstrated an abnormal high T2 signal in the spinal cord grey matter (Fig. 2). Three of these cases showed high T2 signal particularly in the cervical spinal cord, with one case having entire cord involvement. Four of the children also showed signal abnormality in the dorsal pons and medulla. Cerebrospinal fluid results showed an elevated white cell count with a predominantly lymphocytic picture, negative for EV-D68 and negative for other viruses or bacteria.

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Treatment

One case did not receive any treatment other than supportive care and made excellent recovery. No significant improvement in clinical symptoms were observed after use of any treatment. Treatment with antihypertensives was commenced in the two most severely affected cases to control hypertension. All five children required significant input from a multidisciplinary therapy team to manage limb and truncal weakness. Gabapentin was used to control pain with good effect. Clinical psychologists were involved in supporting the children and their families.

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Clinical outcome at 18 months

Clinical progress at 18 months post admission is summarized in Table I. Recovery for affected cases was most significant in the first 12 months; however, they continued to show improvement even beyond this time. One child had recovered almost fully with only mild lower limb weakness and a mild gait abnormality persisting. Two of the most severely affected required long-term home ventilation and were able to manage short periods without ventilation during the day while awake. Both children can feed orally with varying degrees of improvement in bulbar function. The autonomic dysfunction suffered during the early part of their admission resolved fully and antihypertensive therapy stopped. Limb pain lasted 6 months.

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Persisting limb weakness and loss of function was predominantly in the lower limbs for two children and in the upper limbs for three children. Despite improvements, there has been persisting proximal limb weakness with muscle wasting in one or more proximal limbs in all cases apart from one. These four cases have been referred for evaluation for nerve transfer. We could not reliably use any standardized functional scoring system because of their unique pattern of weakness and adaptation. Unlike other motor disorders there seems to be persisting regeneration in some muscle groups.

DISCUSSION

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The confirmed cases in this cluster were linked in time, place, and person and presented to hospital with significant neurological symptoms within a 2-week period. No clear hypothesis for a common environmental exposure was identified in this cluster based on recall of parents or guardians. After the presentation of this cluster we retrospectively retested all throat swabs and NPAs for EV-D68 which had previously tested positive for enterovirus. This retrospective testing found 59 samples between July and October 2016 were positive for EV-D68. These were in a select population of those presenting to hospital, mostly children with respiratory symptoms; however, these positive samples indicate wider circulation of EV-D68 in South East Scotland during this time. The baseline clinical data of those children reported to have EV-D68 without AFM did not identify any potential risk factors for AFM apart from the fact that the AFM cohort were much younger.

The age of presentation, pattern of limb weakness, bulbar involvement, cerebrospinal fluid results, MRI findings, and nerve conduction studies are like other reported case series.^{8-11,13} Two cases with autonomic involvement with severe hypertension and evidence of end organ damage during acute presentation had not been reported before. There was no

association between steroid treatment and subsequent hypertension. One case developed worsening respiratory function after the use of general anaesthetic during lumbar puncture. It is not possible to determine whether this was exacerbated by use of anaesthesia, but we advise caution with use of general anaesthetic for suspected cases in future. We wanted to carry out follow-up MRI studies and we delayed this to avoid general anaesthesia. NPA was found to be the investigation which most consistently identified EV-D68 infection even when the throat swab was negative.

Different treatments (intravenous immunoglobulin, steroids, etc.) have been used in acute settings and the benefits of these treatments are not well understood. Although the numbers are small one case in our cohort made almost full recovery without any treatment. Further studies are needed to establish the benefits of these treatments.

Long-term outcome is variable and in our cohort all children can walk, talk, and feed with varying degrees of persistent neurological deficits at 18 months follow-up. Permanent proximal limb weakness with muscle wasting was present in four cases with varying severity. There seems to be continued improvement even at 18 months and rehabilitation in community settings with psychological support should be provided for future affected cases.

Recent developments have shown that infection with EV-D68 can cause AFM in murine models and the virus has been isolated from the spinal cord of infected mice.¹³ The short duration of prodromal illnesses before onset of acute neurology favours pathogenesis through direct destruction of the nerve by the virus. Direct or indirect association of viruses with neuroinflammatory disorders (N-methyl-D-aspartate, multiple sclerosis, Guillain-Barré syndrome, etc.) are rare but have been increasingly recognized. It is important to try to understand the susceptibility in those affected. This is a case series and hence there are limitations. There is an urgent need for a coordinated, cooperative, international approach to monitoring this emerging infection globally particularly as cases of AFM associated with EV-D68 infection emerge in other regions out with North America and Europe.^{16–18}

CONCLUSIONS

EV-D68 associated AFM present with short prodromal illness, asymmetric limb weakness, bulbar involvement, severe pain, and some autonomic involvement in previously well children, confirmed by MRI and EV-68 viral isolation. This condition has a devastating effect on the physical and mental health of the child and family and there is a lack of any prevention or treatment for complications. There are significant resource implications for health care services; not only in the provision of intensive care but also for long-term home ventilation and community rehabilitation. Further research should be targeted at the prevention of infection as well as understanding and preventing serious sequelae of AFM aiming to minimize complications. To achieve these goals, a global coordinated response from researchers, clinicians, virologists, and public health is required to understand and ultimately prevent this infection and its potential severe neurological sequelae. It is imperative that we act now as outbreaks of EV-D68 and reports of cases of AFM associated with infection become more common.

ACKNOWLEDGMENTS

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SUPPORTING INFORMATION

The following additional material may be found online:

- Appendix S1:** NHS Lothian EV-D68 associated AFM study group.
- Appendix S2:** Parent interview trawling questionnaire.

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Table I: Characteristics of confirmed cases of EV-D68 with associated AFM and clinical features at 18 months follow-up

Clinical details	Case 1	Case 2	Case 3	Case 4	Case 5
Age at onset	2y	5y	4y	6y	2y
Sex	Male	Male	Female	Female	Male
Medical history	Mild asthma	None	None	None	CMPI
Prodromal symptoms (duration in days)	Fever, earache, reduced appetite (5)	Fever, headache, malaise, pyrexia (4)	Fever, headache, vomiting (2)	Fever, cough, headache, reduced appetite (1)	Fever, coryza (7)
Asymmetric severe flaccid limb weakness	Yes	Yes	Yes	Yes	Yes
Limb weakness	UL>LL	LL>UL	UL>LL	UL>LL	LL>UL
Cranial nerve involvement	Yes	No	Yes	Yes	Yes
Bulbar symptoms	Yes	No	Yes	Yes	No
Reduced or absent reflexes	Yes	Yes	Yes	Yes	Yes
Autonomic symptoms	Yes	No	No	Yes	No
Severe pain	Yes	Yes	Yes	Yes	Yes
MRI cord abnormality (location)	Yes (C2–C7)	Yes (C2–C7)	Yes (movement artefact)	Yes (C2–C7)	Yes (entire cord, maximum T1–T2)
MRI abnormality of pons and medulla	Yes	No	No	Yes	Yes
EV-D68 polymerase chain reaction detection	NPA (+) Throat swab (-) CSF (-) Stool (-)	NPA (+) Throat swab (-) Stool (-)	NPA (+) Throat swab (-) Stool (-)	NPA (+) Throat swab (+) Stool (-)	NPA (+) Throat swab (+) CSF (-) Stool (-)
Electromyography	Increased	Not	Not	Increased	Not

(left biceps)	insertional activity, frequent fibrillations. No voluntary activity	performed	performed	insertional activity, widespread fibrillations. Two discrete complex repetitive discharges. No spontaneous activity	performed
Nerve conduction studies	Normal sensory Reduced CMAP	Not performed	Not performed	Normal sensory Early CMAP normal	Not performed
Treatment	IVIG, Steroids	None	IVIG	IVIG	IVIG, steroids
Respiratory support	Yes (long-term invasive ventilation)	No	No	Yes (long-term invasive ventilation)	No
Intensive care support	Prolonged	No	No	Prolonged	Short term
Hospital stay (days)	376	67	125	278	62
At 18mo follow-up					
Mobility	Walking short distances	Walking short distances.	Almost normal mobility.	Walking short distances.	Almost normal mobility.
Speech	Normal	Normal	Normal	Almost normal	Normal
Swallow	Normal	Normal	Normal	Almost normal	Normal
Weakness	Significant proximal upper limb (asymmetric) with muscle wasting	Significant lower limb proximal weakness (asymmetric)	Mild distal unilateral lower limb weakness affecting gait	Significant proximal upper limb (asymmetric) with muscle wasting	Significant proximal upper limb (asymmetric) with muscle wasting
Shoulder dislocation	Yes	No	No	Yes	Yes

Scoliosis	Yes	Yes	No	Yes	No
Head tilt	Yes	No	No	Yes	Yes
Breathing	Tracheostomy and ventilatory support during sleep	Normal	Normal	Tracheostomy and ventilatory support during sleep	Normal

EV-D68, enterovirus D68; AFM, acute flaccid myelitis; CMPI, cow's milk protein intolerance; UL, upper limb; LL, lower limb; MRI, magnetic resonance imaging; NPA, nasopharyngeal aspirate; CSF, cerebrospinal fluid; CMAP, compound muscle action potential; IVIg, intravenous immunoglobulin.

[Figure legends]

Figure 1: Timeline of symptom onset or confirmed cases of acute flaccid myelitis associated with enterovirus D68 infection

Figure 2: Magnetic resonance imaging (MRI) of the spinal cord and brainstem in acute flaccid myelitis caused by enterovirus D68. The sagittal T2-weighted sequences (a,d) showing longitudinal hyperintense signal and the Axial T2-weighted sequences (b,c) showing hyperintensity in spinal cord grey matter (b) and dorsal brainstem (c).

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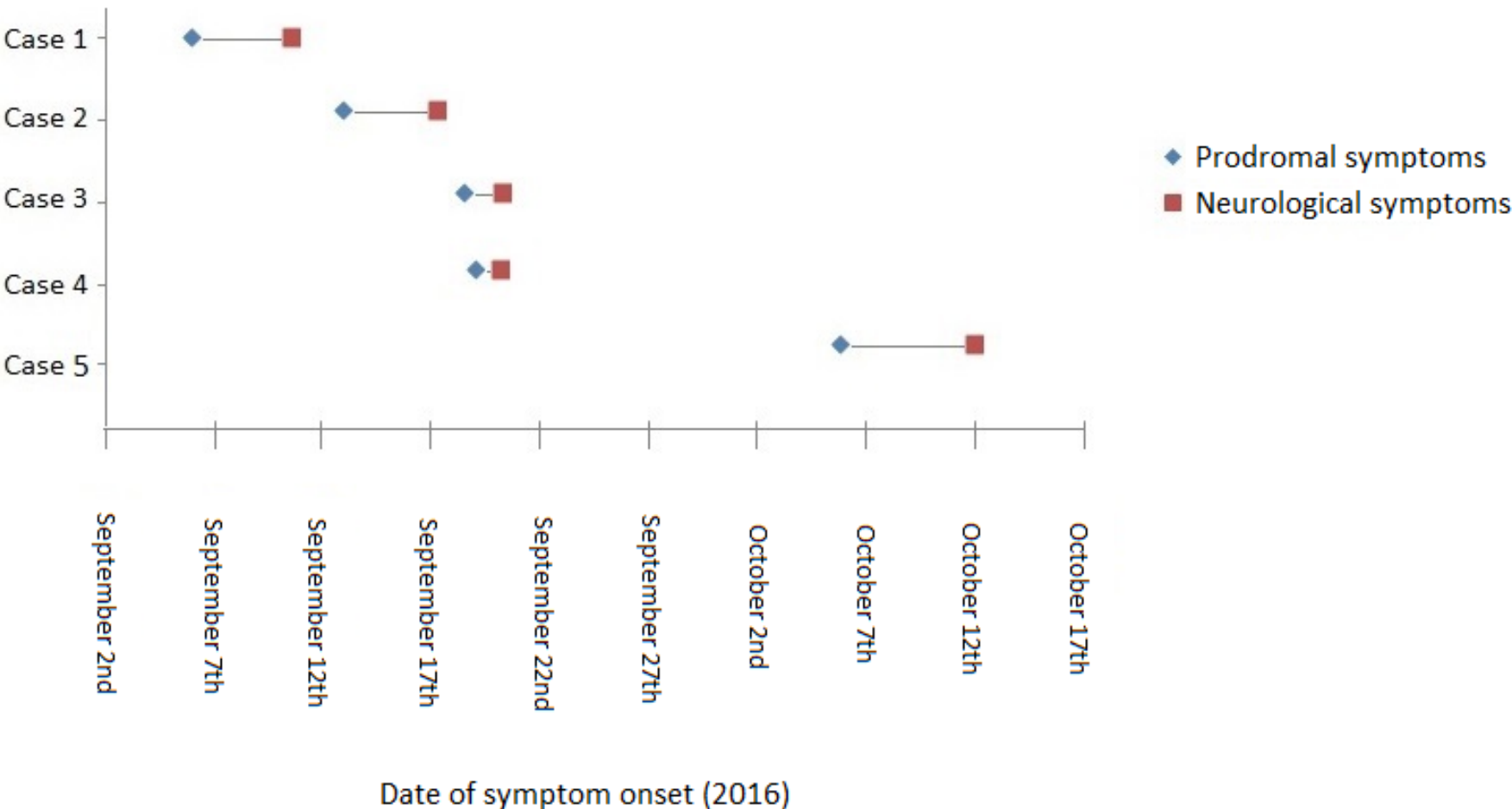
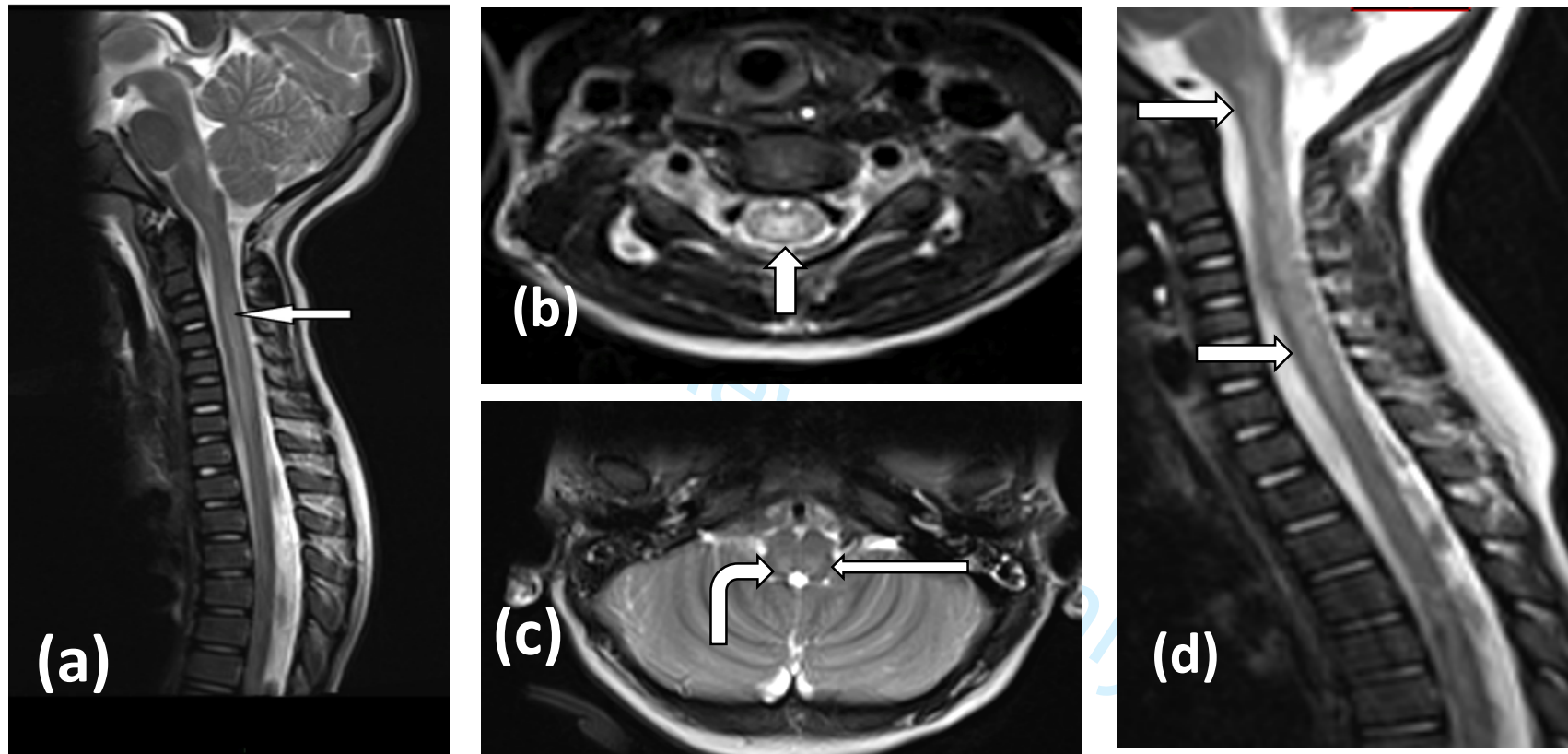


Figure 2. MRI spine and brainstem in AFM due to EV D68- Scotland



Magnetic resonance imaging (MRI) of the spinal cord and brainstem in acute flaccid myelitis caused by enterovirus D68. The sagittal T2-weighted sequences (a,d) showing longitudinal hyperintense signal and the Axial T2-weighted sequences (b,c) showing hyperintensity in spinal cord grey matter (b) and dorsal brainstem (c).

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NHS Lothian Acute Neurologic Illness with Limb Weakness in Children: Form

Form to be completed by or in conjunction with a physician who provided care to the patient during the neurologic illness.

Part 1A Patient details

1. Today's date__/_/____ (dd/mm/yyyy) 2. Name of person completing form:

3. HPT Board _____

4. Name of physician who can provide additional clinical/lab information, if needed

5. Hosp_____ Phone: _____ Email:

6. Patient Name _____

7. CHI _____

8. Patient's Sex ☐ M ☐ F

9. Patient's DOB__/_/____ age: _____ years AND _____ months

10. Patient's home address _____ 11. Post code _____

12. Ethnicity: ☐ Asian/Asian British ☐ Black / African / Caribbean / Black British ☐ Mixed / Multiple ethnic groups ☐ White

12. Date of onset of initial illness __/_/____ Date of onset of any limb weakness: __/_/____ arm / leg

Details _____

Past Medical History _____

13. Was patient admitted to a hospital? ☐ yes ☐ no

14. Date of admission to first hospital__/_/____ Where _____ Date of admission to RHSC __/_/____

Details of general ward _____ HDU or ICU admission ☐ yes ☐ no & dates __/_/____

Ventilated ☐ yes ☐ no Date ventilation started __/_/____ Date came off ventilator __/_/____

.....

Outcome

15. Confirmed Enterovirus D68 ☐ yes ☐ no Sample _____

16. Date of discharge from hospital__/_/____ Discharge to home ☐ yes, another hospital ☐ yes

Details:

Clinical status two months after onset: ☐ At home ☐ still in hospital ☐ improved ☐ not improved ☐ ventilated ☐ Died: __/_/____

Comments :

Case no

Patient Name _____ DOB ____/____/____

PART 1B Epidemiology details completed on ____/____/2016 .Name of Dr completing this bit of the form

Explain-unusual illness in the UK and we would like to gather more information in order to understand the illness better

Family history:

Details of who does the case live with (name/age)

Details of pets in household

Anyone in the household with similar symptoms of intercurrent illness? ☐ yes ☐ no ☐ unknown add details/dates

Details of any contact with anyone else with similar symptoms

Details of nursery playgroup childminder school attended

Details of attendance at any health care waiting rooms eg GP, dentist, A&E

Vaccination history:Are they up to date according to UK childhood schedule? ☐ yes ☐ no ☐ unknown

44. How many doses of **inactivated polio vaccine (IPV)** are **documented** to have been received by the patient before the onset of weakness? & when

_____doses ☐ unknown

45. How many doses of **oral polio vaccine (OPV)** are **documented** to have been received by the patient before the onset of weakness? & when

_____doses ☐ unknown46. If you do not have documentation of the *type* of polio vaccine received:What is total number of **documented** polio vaccine doses received before onset of weakness?_____doses ☐ unknown

47. Details of last vaccination received & when?

48. Flu vaccine details what when?

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TRAVEL IN UK AND ABROAD in 4 weeks pre-onset of limb weakness		Yes	No	NS
1. Spent any nights away from home WITHIN THE UK? <i>(Holidays or business trips; staying at friends or relatives, hotels, campsites, etc)</i>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
IF YES: Please state dates and where	From: ____/____/____ To: ____/____/____			
Address visited, including postcode:	_____			
2. Spent any nights away from home OUTSIDE THE UK <i>(Holidays or business trips; staying at friends or relatives, hotels, campsites, etc)</i>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
IF YES: Please state dates and country/resort	From: ____/____/____ To: ____/____/____			
Country and resort:	_____			
Environmental exposures: in the 4 weeks before onset, has the patient:		Yes	No	Unk
Swam or played in a swimming pool, indoor or outdoor? If Yes, details:		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Taken part in water sports including sailing, canoeing, windsurfing, fishing? If Yes, details:		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Taken part in any outdoor activity that brought them into contact with forest, soil, mud or water-courses in fields or open land, including hill-walking, mountain-biking and canoeing? If Yes, details:		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Any insect bites (including tick bites) ? If Yes, details:		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Worked/played in a garden or allotment (including usual home gardening)? If Yes, details:		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Used or had contact with any household chemical for cleaning (e.g. bleach, cleaning sprays)? If Yes, details:		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Used or had contact with any garden chemicals, such as weedkillers, insecticides? If Yes, details:		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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Patient Name _____ DOB ____/____/____

	Yes	No	Unk
Food and drink exposures: In the 4 weeks before onset, has the patient:			
Eaten any meals/ snacks bought from fast-food outlets? Fast-food outlets include any restaurant, stall or shop where food is paid for before it is eaten, such as sandwich bars, canteens, burger bars, kebab shops, fish and chip shops, hot dog stands, food outlets at markets	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Eaten any meals or snacks from any other restaurants, cafes, pubs or hotels?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Eaten any meals or snacks at any function or gathering, e.g. at a party, reception, barbecue, picnic, etc?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Eat any meals/snacks bought from grocers, bakers, supermarkets or delicatessens which were consumed away from the premises?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Eaten any fish or shellfish?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Eaten any tinned food?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Eaten any new, unusual or imported foods? (e.g. wild berries, teas)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Used any Chinese or herbal medicines etc (details)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
If yes to any of the above, please add details of premises, food items and dates consumed			

Patient Name _____ DOB / /

Places visited or any social gatherings in 14 days prior to onset of initial illness DOO / /

(Family might want to take this away and complete)

[illegible]

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Patient Name _____ DOB ____/____/____

PART 2 Virology testing: details completed on ____/____/2016 .Name of Dr completing this bit of the form:

73. Was CSF tested for the following pathogens?	Date of specimen collection ____/____/____ <input type="checkbox"/> Not done	ID _____
	Enterovirus PCR: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done If positive: type: <input type="checkbox"/> Not typed	
	Herpes Simplex Virus PCR: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done	
	Cytomegalovirus PCR: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done	
	Varicella Zoster Virus PCR: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done	
	Other pathogen identified: specify: Type of test:	

74. Was a respiratory tract specimen tested for the following pathogens?	Date of specimen collection ____/____/____ <input type="checkbox"/> Not done
Page 4 of 6	Enterovirus/rhinovirus PCR: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done If positive: type: <input type="checkbox"/> Not typed
Page 4 of 6	Adenovirus PCR: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done If positive: type: <input type="checkbox"/> Not typed
	Influenza virus PCR: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done If positive: type: <input type="checkbox"/> Not typed
	Other pathogen identified: specify: Type of test:

75. Was a stool specimen tested for the following pathogens?	Date of specimen collection ____/____/____ <input type="checkbox"/> Not done
	Enterovirus PCR: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done If positive: type: <input type="checkbox"/> Not typed
	Poliovirus PCR: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done

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	Poliovirus culture: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done
	Other pathogen identified: specify: Type of test:

76. Was serum tested for the following pathogens?	Date of specimen collection ____/____/____ <input type="checkbox"/> Not done
	West Nile Virus: <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not done If positive, test type: <input type="checkbox"/> IgM <input type="checkbox"/> PCR
	Other pathogen identified: specify: Type of test:

77. Describe any other laboratory finding(s) considered to be significant _____

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PART 3 Clinical **Neurological details completed on** ____/____/2016 .Name of Dr completing this bit of the form:**17. Signs/symptoms/condition at ANY time during the illness:**

Date of onset of limb weakness: ____/____/____

	Right Arm	Left Arm	Right Leg	Left Leg
18. Since neurologic illness onset, which limbs have been acutely weak? [indicate yes(y), no (n), unknown (u) for each limb]	Y N U	Y N U	Y N U	Y N U
19. Date of neurologic exam (recorded at worst weakness thus far) (dd/mm/yyyy)	____/____/____			
20. Reflexes in the affected limb(s): (recorded at worst weakness thus far)	<input type="checkbox"/> Areflexic/hyporeflexic (0-1) <input type="checkbox"/> Normal (2) <input type="checkbox"/> Hyperreflexic (3-4+)			
21. Any sensory loss/numbness in the affected limb(s), at any time during the illness? (paresthesias should not be considered here)	Y N U			
22. Any pain or burning in the affected limb(s)? (at any time during illness)	Y N U	Y N U	Y N U	Y N U
			Yes	No
23. Sensory level on the torso (ie, reduced sensation below a certain level of the torso)? (at any time during illness)				Unknown
24. At any time during the illness, please check if the patient had any of the following cranial nerve signs:				
<input type="checkbox"/> Diplopia/double vision (If yes, circle the cranial nerve involved if known: 3 / 4 / 6)				
<input type="checkbox"/> Loss of sensation in face <input type="checkbox"/> Facial droop <input type="checkbox"/> Hearing loss <input type="checkbox"/> Dysphagia <input type="checkbox"/> Dysarthria				
25. Any pain or burning in neck or back? (at any time during illness)				
26. Bowel or bladder incontinence? (at any time during illness)				
27. Cardiovascular instability (e.g, labile blood pressure, alternating tachy/bradycardia)? (at any time during illness)				
28. Change in mental status (e.g, confused, disoriented, encephalopathic)? (at any time during illness)				
29. Seizure(s)? (at any time during illness)				
30. Received care in ICU because of neurologic condition? (at any time during illness)				
31. Received invasive ventilatory support (e.g, intubation, tracheostomy) because of neurological condition?				

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Within the 4-week period BEFORE onset of limb weakness, did patient:	Yes	No	Unkn	
32. Have a respiratory illness?				33. If yes, date of onset __/__/____ & details of symptoms
34. Have a fever, measured by parent or provider and ≥ 38.0°C?				35. If yes, date of onset __/__/____
36. Receive oral, IM or IV steroids?				
37. Receive any other systemic Immunosuppressant(s)?				38. If yes, list:
41. Does patient have any underlying illnesses? Past Medical History				42. If yes, list
43. On the day of onset of limb weakness, did patient have a fever? (see definition above)				

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Patient Name _____ DOB ____/____/____

Neuroradiographic findings: (Indicate based on most abnormal study)**MRI of spinal cord** 47. Date of study ____/____/____ (mm/dd/yyyy)48. Levels imaged: ☐cervical ☐thoracic ☐lumbosacral ☐unknown49. Gadolinium used? ☐yes ☐no ☐unknown

50. Location of lesions:	<input type="checkbox"/> cervical cord <input type="checkbox"/> conus <input type="checkbox"/> unknown	<input type="checkbox"/> thoracic cord <input type="checkbox"/> cauda equina	Levels of cord affected (if applicable): 51. Cervical: _____ 52. Thoracic: _____
For cervical and thoracic cord lesions	53. What areas of spinal cord were affected?	<input type="checkbox"/> predominantly gray matter <input type="checkbox"/> both equally affected	<input type="checkbox"/> predominantly white matter <input type="checkbox"/> unknown
	54. Was there cord edema?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown	
For cervical, thoracic cord or conus lesions	55. Did any lesions enhance with GAD?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown	
For cauda equina lesions	56. Did the ventral nerve roots enhance with GAD?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown	
	57. Did the dorsal nerve roots enhance with GAD?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown	ID _____

MRI of brain 62. Date of study ____/____/____ (dd/mm/yyyy)58. Gadolinium used? ☐yes ☐no ☐unknown

59. Any supratentorial (i.e. lobe, cortical, subcortical, basal ganglia, or thalamic) lesions	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown	
	60. If yes, indicate location(s)	<input type="checkbox"/> cortex <input type="checkbox"/> subcortex <input type="checkbox"/> basal ganglia <input type="checkbox"/> thalamus <input type="checkbox"/> unknown
	61. If yes, did any lesions enhance with GAD?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown
62. Any brainstem lesions?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown	
	63. If yes, indicate location:	<input type="checkbox"/> midbrain <input type="checkbox"/> pons <input type="checkbox"/> medulla <input type="checkbox"/> unknown
	64. If yes, did any lesions enhance with GAD?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown
65. Any cranial nerve lesions?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown	
	66. If yes, indicate which CN(s):	CN _____ <input type="checkbox"/> unilateral <input type="checkbox"/> bilateral CN _____ <input type="checkbox"/> unilateral <input type="checkbox"/> bilateral CN _____ <input type="checkbox"/> unilateral <input type="checkbox"/> bilateral CN _____ <input type="checkbox"/> unilateral <input type="checkbox"/> bilateral
	67. If yes, did any lesions enhance with GAD?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown
68. Any lesions affecting the cerebellum ?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown	

69. Was an EMG done? ☐yes ☐no ☐unknown If yes, date ____/____/____ (mm/dd/yyyy)70. If yes, was there evidence of acute motor neuropathy, motor neuronopathy, motor nerve or anterior horn cell involvement? ☐yes ☐no ☐unkn

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Patient Name_____DOB__/_/____

CSF examination: 71. Was a lumbar puncture performed? ☐yes ☐no ☐unknown If yes, complete 72 (If more than 2 CSF examinations, list earliest and then most abnormal)

	Date of lumbar puncture	WBC/mm3	% neutrophils	% lymphocytes	% monocytes	% eosinophils	RBC/mm3	Glucose mg/dl	Protein mg/dl
72a. CSF from LP1									
72b. CSF from LP2									

71. Any other significant details of clinical illness?